Clinical Policy: Patisiran (Onpattro)

Reference Number: PA.CP.PHAR.395
Effective Date: 10/2018
Last Review Date: 04/2025

Description
Patisiran (Onpattro®) is a transthyretin (TTR)-directed small interfering ribonucleic acid.

FDA Approved Indication(s)
Onpattro is indicated for the treatment of the polyneuropathy of hereditary TTR-mediated amyloidosis in adults.

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of PA Health & Wellness® that Onpattro is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Hereditary Transthyretin-Mediated Amyloidosis (must meet all)**:**

1. Diagnosis of hereditary TTR-mediated amyloidosis with polyneuropathy;
2. Documentation confirms presence of a TTR mutation;
3. Biopsy is positive for amyloid deposits or medical justification is provided as to why treatment should be initiated despite a negative biopsy or no biopsy;
4. Prescribed by or in consultation with a neurologist;
5. Age ≥ 18 years;
6. Member has not had a prior liver transplant;
7. Onpattro is not prescribed concurrently with Amvuttra™, Tegsedi™ or Wainua™;
8. Dose does not exceed the following (based on actual body weight):
   a. Weight < 100 kg: 0.3 mg/kg once every 3 weeks;
   b. Weight ≥ 100 kg: 30 mg once every 3 weeks.

Approval duration: 6 months

B. Other diagnoses/indications

1. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53.

II. Continued Therapy

A. Hereditary Transthyretin-Mediated Amyloidosis (must meet all)**:**

1. Currently receiving medication via PA Health & Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care Policy (PA.PHARM.01) applies;
2. Member is responding positively to therapy [e.g., improved measures of polyneuropathy (e.g., motor strength, sensation, and reflexes), improvement in quality

of life, motor function, walking ability (e.g., as measured by timed 10-m walk test), and nutritional status (e.g., as evaluated by modified mass index)];
3. Member has not had a prior liver transplant;
4. Onpattro is not prescribed concurrently with Amvuttra, Tegsedi, or Wainua ;
5. If request is for a dose increase, new dose does not exceed the following (based on actual body weight):
   a. Weight < 100 kg: 0.3 mg/kg once every 3 weeks;
   b. Weight ≥ 100 kg: 30 mg once every 3 weeks.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via PA Health & Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care Policy (PA.PHARM.01) applies.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policy – PA.CP.PMN.53 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
FDA: Food and Drug Administration
TTR: transthyretin

Appendix B: Therapeutic Alternatives
Not applicable

Appendix C: Contraindications/Boxed Warnings
None reported

Appendix D: General Information
- To confirm amyloidosis, the demonstration of amyloid deposits via tissue biopsy is essential. Deposition of amyloid in the tissue can be demonstrated by Congo red staining of biopsy specimens. With Congo red staining, amyloid deposits show a characteristic green birefringence under polarized light; however, negative biopsy results should not be interpreted as excluding the disease.
- DNA sequencing is usually required for genetic confirmation. Current techniques for performing sequence analysis of TTR, the only gene known to be associated with TTR amyloidosis, detect >99% of disease-causing mutations.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Hereditary transthyretin-mediated amyloidosis-associated polyneuropathy	• Adults weighing < 100 kg: 0.3 mg/kg IV every 3 weeks • Adults weighing ≥ 100 kg: 30 mg IV every 3 weeks • Premedicate with a corticosteroid, acetaminophen, and antihistamines to reduce the risk of infusion-related reactions. • Onpattro should be administered by a healthcare professional.	See dosing regimen

VI. Product Availability

Lipid complex injection (single-dose vial): 10 mg/5 mL (2 mg/mL)

VII. References

1. Onpattro Prescribing Information. Cambridge, MA: Alnylam Pharmaceuticals, Inc.; January 2023. Available at: https://www.alnylam.com/sites/default/files/pdfs/ONPATTRO-Prescribing-Information.pdf. Accessed January 17, 2025.
2. Ando Y, Coelho T, Berk JL, et al. Guideline of transthyretin-related hereditary amyloidosis for clinicians. Orphanet J Rare Dis. 2013 Feb 20;8:31.
3. Adams D, Gonzalez-Duarte A, O'Riordan WD, et al. Patisiran, an RNAi Therapeutic, for Hereditary Transthyretin Amyloidosis. N Engl J Med. 2018 Jul 5;379(1):11-21.
4. Magrinelli F, Fabrizi GM, Santoro L, et al. Pharmacological treatment for familial amyloid polyneuropathy. Cochrane Database Syst Rev. 2020;4(4):CD012395.
5. Alcantara M, Mezei MM, Baker SK, et al. Canadian guidelines for hereditary transthyretin amyloidosis polyneuropathy management. Can J Neurol Sci. 2022;49(1):7-18.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J0222	Injection, patisiran, 0.1 mg

Reviews, Revisions, and Approvals	Date
Policy created	10/2018
4Q 2019 annual review: No changes per Statewide PDL implementation 01-01-2020	10/2019
4Q 2020 annual review: genetic testing methodology examples removed from criteria with deference to appendix; references reviewed and updated.	08/2020
4Q 2021 annual review: added requirement that Onpattro is not prescribed concurrently with Tegsedi; added biopsy requirement to align with	10/2021

Reviews, Revisions, and Approvals	Date
previously Corporate P&T-approved approach for this class of medications; references reviewed and updated.	
4Q 2022 annual review: added criterion for no prior treatment with Amvuttra or Tegsedi in initial approval criteria due to lack of supportive evidence; updated concurrent use exclusion with recently approved TTR-directed small interfering ribonucleic acid Amvuttra for both initial and continued approval criteria; included criterion for no prior liver transplant for continued approval criteria (already exists in initial approval criteria); references reviewed and updated.	10/2022
4Q 2023 annual review: no significant changes; references reviewed and updated.	10/2023
2Q 2024 annual review: added Wainua to list of drugs that should not prescribed concurrently; references reviewed and updated.	04/2024
2Q 2025 annual review: no significant changes; references reviewed and updated.	04/2025